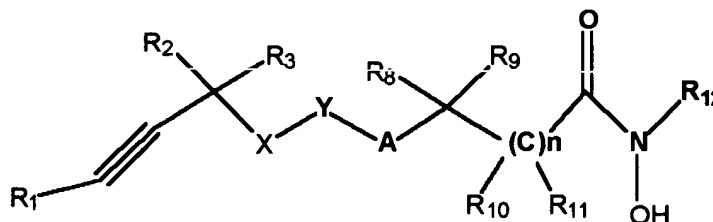


AMENDMENT TO THE CLAIMS

Claim 1 (currently/previously amended). A compound of formula



I

wherein:

R₁ is hydrogen, aryl, heteroaryl, alkyl of 1-8 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, or -C₄-C₈-cycloheteroalkyl;

R₂ and R₃ are each, independently, hydrogen, alkyl of 1-6 carbon atoms, -CN, or -CCH₃;

R₇ is hydrogen, aryl, aralkyl, heteroaryl, heteroaralkyl, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 1-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, -C(O)-R₁, -SO₂-R₁, -C(O)-NHR₁, -C(O)NR₃R₆, -C(O)R₁NR₃R₆, -C(O)-OR₁, ~~-C(NH)=NH₂~~, or -C(NH)-NH₂;

R₈, R₉, R₁₀, and R₁₁ are each, independently, hydrogen, aryl or heteroaryl, cycloalkyl of 3-6 carbon atoms, -C₄-C₈-cycloheteroalkyl, alkyl of 1-18 carbon atoms, alkenyl of 2-18 carbon atoms, alkynyl of 2-18 carbon atoms; with the proviso that one of the pairs R₈ and R₉, R₉ and R₁₀ or R₁₀ and R₁₁, together with the carbon atom or atoms to which they are attached, form a cycloalkyl ring of 3-6 carbon atoms, or a -C₄-C₈-cycloheteroalkyl ring;

R₁₂ is hydrogen, aryl or heteroaryl, cycloalkyl of 3-6 carbon atoms, -C₄-C₈-cycloheteroalkyl, or alkyl of 1-6 carbon atoms;

A is O, S, SO, SO₂, NR₇, or CH₂;

X is O, S, SO, SO₂, NR₇, or CH₂;

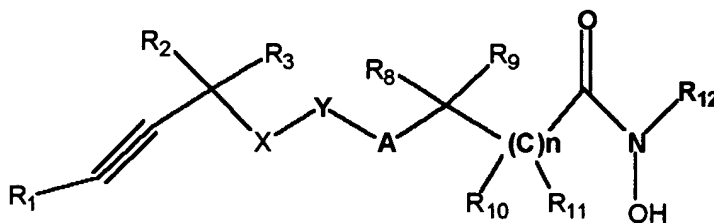
Y is aryl or heteroaryl, with the proviso that A and X are not bonded to adjacent atoms of Y; and with the further proviso that if Y is phenyl, then R₈ and R₉ together with the carbon atom to which they are attached may not form a piperdinyll or tetrahydropyranyll ring; and

n is 0-2; or a pharmaceutically acceptable salt thereof.

Claim 2 (currently amended). A compound of Claim 1 wherein Y is phenyl, pyridyl, thienyl, furanyl, imidazolyl, ~~or~~ triazolyl or thiadiazolyl.

Claim 3 (canceled).

Claim 4 (currently/previoursly amended). A method of ~~treating a pathological condition or disorder which requires inhibition of~~ inhibiting pathological changes mediated by TNF- α converting enzyme (TACE) in a mammal in need thereof which comprises administering to said mammal a therapeutically effective amount of a compound having the formula



wherein:

R₁ is hydrogen, aryl, heteroaryl, alkyl of 1-8 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, or -C₄-C₈-cycloheteroalkyl;

R₂ and R₃ are each, independently, hydrogen, alkyl of 1-6 carbon atoms, -CN, or -CCH₃;

R₇ is hydrogen, aryl, aralkyl, heteroaryl, heteroaralkyl, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 1-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, -C(O)-R₁, -SO₂-R₁, -C(O)-NHR₁, -C(O)NR₅R₆, -C(O)R₁NR₅R₆, -C(O)-OR₁, -C(NH)-NH₂, or -C(NH)-NH₂;

R₈, R₉, R₁₀, and R₁₁ are each, independently, hydrogen, aryl or heteroaryl, cycloalkyl of 3-6 carbon atoms, -C₄-C₈-cycloheteroalkyl, alkyl of 1-18 carbon atoms, alkenyl of 2-18 carbon atoms, alkynyl of 2-18 carbon atoms; with the proviso that one of the pairs R₈ and R₉, R₉ and R₁₀ or R₁₀ and R₁₁, together with the carbon atom or atoms to which they are attached, form a cycloalkyl ring of 3-6 carbon atoms, or a -C₄-C₈-cycloheteroalkyl ring;

R₁₂ is hydrogen, aryl or heteroaryl, cycloalkyl of 3-6 carbon atoms, -C₄-C₈-cycloheteroalkyl, or

alkyl of 1-6 carbon atoms;

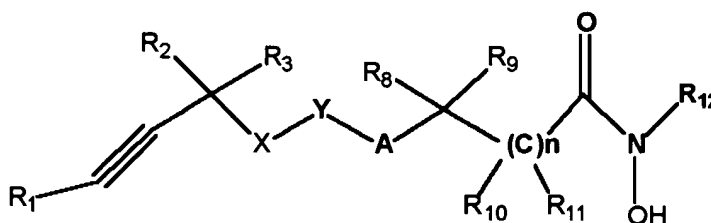
A is O, S, SO, SO₂, NR₇, or CH₂;

X is O, S, SO, SO₂, NR₇, or CH₂;

Y is aryl or heteroaryl, with the proviso that A and X are not bonded to adjacent atoms of Y; and with the further proviso that if Y is phenyl, then R₈ and R₉ together with the carbon atom to which they are attached may not form a piperdinyll or tetrahydropyranyl ring; and n is 0-2; or a pharmaceutically acceptable salt thereof.

Claim 5 (original). The method of Claim 4 wherein the condition treated is rheumatoid arthritis, graft rejection, cachexia, inflammation, fever, insulin resistance, septic shock, congestive heart failure, inflammatory disease of the central nervous system, inflammatory bowel disease or HIV infection.

Claim 6 (currently/previously amended). A pharmaceutical composition comprising a therapeutically effective amount of a compound having the formula



wherein:

R₁ is hydrogen, aryl, heteroaryl, alkyl of 1-8 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, or -C₄-C₈-cycloheteroalkyl;

R₂ and R₃ are each, independently, hydrogen, alkyl of 1-6 carbon atoms, -CN, or -CCH₃;

R₇ is hydrogen, aryl, aralkyl, heteroaryl, heteroaralkyl, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 1-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, -C(O)-R₁, -SO₂-R₁, -C(O)-NHR₁, -C(O)NR₅R₆, -C(O)R₁NR₅R₆, -C(O)-OR₁, -C(NH)-NH₂, or -C(NH)-NH₂;

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R₈, R₉, R₁₀, and R₁₁ are each, independently, hydrogen, aryl or heteroaryl, cycloalkyl of 3-6 carbon atoms, -C₄-C₈-cycloheteroalkyl, alkyl of 1-18 carbon atoms, alkenyl of 2-18 carbon atoms, alkynyl of 2-18 carbon atoms; with the proviso that one of the pairs R₈ and R₉, R₉ and R₁₀ or R₁₀ and R₁₁, together with the carbon atom or atoms to which they are attached, form a cycloalkyl ring of 3-6 carbon atoms, or a -C₄-C₈-cycloheteroalkyl ring;

R₁₂ is hydrogen, aryl or heteroaryl, cycloalkyl of 3-6 carbon atoms, -C₄-C₈-cycloheteroalkyl, or alkyl of 1-6 carbon atoms;

A is O, S, SO, SO₂, NR₇, or CH₂;

X is O, S, SO, SO₂, NR₇, or CH₂;

Y is aryl or heteroaryl, with the proviso that A and X are not bonded to adjacent atoms of Y; and with the further proviso that if Y is phenyl, then R₈ and R₉ together with the carbon atom to which they are attached may not form a piperdinyll or tetrahydropyranyll ring; and

n is 0-2; or a pharmaceutically acceptable salt thereof.